Citation:

He J, Gu D, Chen J, Jaquish CE, Rao DC, Hixson JE, Chen JC, Duan X, Huang JF, Chen CS, Kelly TN, Bazzano LA, Whelton PK; GenSalt Collaborative Research Group. Gender difference in blood pressure responses to dietary sodium intervention in the GenSalt study. *J Hypertens.* 2009 Jan; 27(1): 48-54.

PubMed ID: 19145767

Study Design:

Non-randomized trial

Class:

M - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine factors related to blood pressure (BP) responses to dietary sodium and potassium intervention.

Inclusion Criteria:

- Participants of the GenSalt study
- Age: 18 to 60 years
- Systolic blood pressure (SBP): 130 to 160mmHg
- Diastolic blood pressure (DBP): 85 to 100mmHg
- Offspring and siblings of those meeting the above criteria.

Exclusion Criteria:

- Stage 2 hypertension (HTN)
- Secondary HTN
- Cardiovascular disease
- Diabetes
- Taking anti-hypertensive drugs
- Pregnant
- Heavy alcohol abuse
- Currently on a low-sodium diet.

Description of Study Protocol:

Recruitment

Participants of the GenSalt study whose BP was 130 to 160mmHg SBP and 85 to 100mmHg DBP were recruited for the dietary study, as well as siblings and offspring of those who qualified.

Design

- Standard questionnaire designed to collect demographics, personal and family history and lifestyle risk factors was administered by trained personnel
- Subjects received either a:
  - Low-salt diet of 3g salt or 51.3mmol sodium for seven days
  - High-salt diet of 18g or 307.8mmol sodium for seven days
  - High-sodium diet plus 60mmol potassium supplement daily for seven days
- Subjects had sitting BP measured three times according to accepted standards at baseline, and the last three days of each intervention phase
- Three-timed urine specimens were obtained (one 24-hour test and two overnight) at baseline and in each phase of the dietary intervention.

Dietary Intake/Dietary Assessment Methodology

- All foods were cooked without salt
- Salt was added to food prior to eating by supervisory staff
- All meals were eaten at the study kitchen under supervision of study staff
- Food consumption of study participants was recorded at each meal.

Blinding Used

Staff measuring BP were blinded to diet that participants were taking.

Intervention

- Three-day run-in
- Seven-day low sodium diet (51.3mmol per day)
- Seven-day high sodium diet (307.8mmol per day)
- Seven-day high sodium diet plus potassium supplement (307.8mmol sodium and 60mmol potassium per day).

Statistical Analysis

- Blood pressure levels were calculated as the mean of nine measurements from the three clinical visits during baseline observation or on days five, six and seven of each intervention phase
- Means and percentages of baseline characteristics were presented by sex and the statistical significance levels were examined by T-test for continuous variables and X^2 for categorical variables
- Differences in urinary excretion of sodium and potassium and BP levels by sex and dietary interventions were examined using two-way analysis of variance
- Multiple linear regression analyses were used to examine the association between BP responses and dietary interventions and sex, age and baseline BP levels.

Data Collection Summary:

Timing of Measurements

Blood pressure, 24-hour urine and two-night urine collections were taken at three baseline clinic observation days and day five, six and seven of each observation study.

Dependent Variables

- *Variable 1:* Three sitting BP measurements were taken by trained personnel at each clinic visit using random-zero sphygmomanometer according to common protocol
- *Variable 2:* Urinary sodium and potassium excretion measured by 24-hour collection and two 12-hour collections.

Independent Variables

- Seven-day low-sodium diet
- Seven-day high-sodium diet
- Seven-day high-sodium diet with potassium supplement daily.

Control Variables

- Sex
- Age
- BMI
- Education
- Alcohol consumption
- Cigarette smoking
- Physical activity.

Description of Actual Data Sample:

- *Initial N:* 1,906 (1,010 males, 896 females)
- *Age:* 18 to 60 years
- *Ethnicity:* Chinese
- *Other relevant demographics:* See table below
- *Anthropometrics:* See table below
- *Location:* Rural areas in norther China.

Table 1. Baseline Characteristics of 1,906 Dietary Sodium and Potassium Intervention Participants

	Men (N=1,010)	Women (N=996)	P for Difference
Age, years	39.3±9.6	38.1±9.4	0.008
Secondary school or higher (percent)	81.1	54.0	<0.0001
Married (percent)	91.1	92.8	0.22
Current alcohol drinkers (percent)	52.9	3.0	<0.0001
Current cigarette smoking (percent)	58.7	0.2	<0.0001
Physical activity (MET)	68.2±22.1	58.7±18.6	<0.0001
BMI (kg/m^2)	23.1±3.1	23.5±3.2	0.009
BMI ≥ 25kg/m^2	26.9	28.4	0.48
Waist circumference (cm)	81.9± 9.9	78.4±9.5	<0.0001
SBP (mmHg)	118.7±12.8	114.9±15.4	<0.0001
DBP (mmHg)	75.6±9.9	71.7±10.5	<0.0001
BP ≥ 140/90 mmHg (percent)	10.8	8.1	0.05

Values are mean ±SD or percentage, BP, blood pressure MET, metabolic equivalent per week.

Summary of Results:

Table 3. Mean Systolic and Diastolic Blood Pressure at Baseline and During Dietary Intervention

Blood Pressure (mmHg)	Men	Women	P for Difference by Sex	P for Differences by Intervention[a]	P for Intervention
Baseline					
SBP	118.7±12.8	114.9±15.6	<0.0001		
DBP	75.6±9.9	71.7±10.5	<0.0001		
Low salt intervention					
SBP	113.3±11.1	109.3±13	<0.0001	<0.0001	0.0002
DBP	73.1±9.3	68.6±9.5	<0.0001	<0.0001	0.0003
High salt intervention					
SBP	117.8±12.1	114.5±15.0	<0.0001	<0.0001	<0.0001
DBP	74.5±9.9	71.1±10.3	<0.0001	<0.0001	0.001
High salt intervention and potassium supplementation					
SBP	114.2±11.6	111.1±14.3	<0.0001	<0.0001	<0.0001
DBP	73.4±9.5	69.4±9.9	<0.0001	<0.0001	0.001

Values are mean SD or percentage; DBP, diastolic blood pressure; SBP, systolic blood pressure. [a]P values are for low-salt intervention compared with baseline, high-salt intervention compared with low-salt intervention or potassium supplementation and high-salt diet compared with high-salt diet.

Table 4. Multivariable-adjusted[a] Mean Changes (95% CI) in Systolic and Diastolic Blood Pressure in Response to Low-salt, High-salt and Potassium-supplementation Interventions by Sex, Age and Baseline Blood Pressure

	Low-sodium Diet		High-sodium Diet		Potassium Supplementation	
	ΔSBP	**ΔDBP**	**ΔSBP**	**ΔDBP**	**ΔSBP**	**ΔDBP**
Sex						
Men	-7.05(-7.5,6.59)	-3.39(-3.77,-3.01)	5.25(4.83,5.66)	1.74(1.36,2.13)	-4.43(-4.82,-4.04)	-1.52(-1.85,-1.19)
Women	-8.07(-8.57,-7.58)	-4.51(-4.02,-4.09)	6.35 (5.9,6.81)	3.08(2.66,3.50)	-4.45(4.88,-4.03)	-2.1(-2.46,-1.74)
P for differences by sex	0.0004	<0.0001	<0.0001	<0.0001	0.93	0.007
Age (years)						
Less than 35	-6.04(-6.64,-5.44)	-4.05(-4.56,-3.55)	4.31(3.75,4.86)	2.00(1.49,2.51)	-3.88(4.40,3.36)	-1.62(-2.26,-1.38)
35 to 44	-7.59(-8.08,-7.10)	-4.01(-4.42,3.59)	5.73(5.28,6.19)	2.57(2.15,2.99)	-4.01(-4.43,-3.58)	-1.75(-2.10,-1.39)
More than 44	-9.05(-9.62,-8.47)	-3.78(-4.27,-3.29)	7.36(6.83,7.89)	2.66(2.17,3.16)	-5.44(-5.94,-4.93)	-1.86(2.29,1.44)
P for differences by age	<0.0001	0.66	<0.0001	0.08	<0.0001	0.90
Baseline BP						
Less than 120/80 mmHg	-3.28(-3.66,2.90)	-1.46(-1.78,-1.14)	4.14(3.79,4.49)	1.44(1.12,1.77)	-2.89(-3.22,-2.56)	-1.14(-1.42,-0.86)
120 to 139/80 to 89 mmHg	-7.57(-8.06,-7.08)	-4.02(-4.43,-3.61)	5.52(5.07,5.98)	2.40(1.08,2.82)	-4.04(-4.47,-3.61)	-1.60(-1.96,-1.23)
140/90 mmHg or more	-11.8(-12.8,-10.9)	-6.36(-7.15,-5.57)	7.74(6.88,8.60)	3.38(2.58,4.18)	-6.40(-7.21,-5.59)	-2.69(-3.38,-2.00)
P-value by differences by baseline BP	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0002

Blood pressure response (95% CI) (mmHg)[b]. BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure. [a]Adjusted for age, sex, baseline BP, BMI, education, alcohol consumption, current smoking, physical activity and baseline 24-hour urinary excretion of sodium and potassium. [b]BP response to low-sodium diet=BP on low-sodium diet - BP at baseline; BP response to high-sodium diet=BP on high-sodium diet - BP on low sodium diet; and BP response to potassium supplementation=BP on high-sodium diet with potassium supplementation - BP on high-sodium diet.

Other Findings

- Urinary excretion of sodium, potassium and creatinine during dietary intervention was consistent with adherence to study protocol
- BP did not decrease in 23.2% of participants during low-sodium diet
- BP did not decrease in 30.6% of participants during potassium supplementation

- BP did not increase in 26.1% of participants during high-salt diet.

Author Conclusion:

- The current study suggests that female gender, older age and elevated baseline BP levels increase BP responses to dietary sodium intervention
- Elevated baseline BP levels increase BP responses to dietary potassium intervention. Therefore, a diet low in sodium and high in potassium should be especially effective in reducing BP among persons with hypertension or pre-hypertension, whereas a diet low in sodium may be more effective in reducing BP among women and the elderly.

Reviewer Comments:

- *2.2: The mean BP of the study participants in Table 1 is lower than what the inclusion criteria would indicate. A probable explanation for this is that the initial selection was of individuals with borderline high BP but their siblings and offspring were also recruited for the study. This was not explained in detail in the text*
- *4.2: No drop-out statistics were reported*
- *5.1: Staff delivering food and participants unable to be blinded but staff taking BP were*
- *6.3: This was only a seven-day intervention with no washout period between trials; interventions were extreme changes in diet. This was identified as a limitation of the study in the discussion.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	N/A
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	???
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes

3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	Yes
4.	**Was method of handling withdrawals described?**	No
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	Yes
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	N/A
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	Yes

7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	???
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes